REMARKS

PRIORITY

Applicants submit that certified copies of the priority documents were provided to the PCT during the processing of priority document PCT/IB00/00830. Thus, no certified copies are deemed necessary. Copies of these certified documents are provided herewith.

THE OATH/DECLARATION

The Examiner has requested a new oath or declaration with the correct title of the invention. An executed Declaration with the correct title of the invention is provided herewith.

DRAWINGS

In response to the Draftperson's objections to the drawings, proposed drawings are provided herewith.

THE AMENDMENTS

Applicants cancel claims 17 through 41 and 43 through 46, and add new claims 48 through 81 (33 total claims) which correspond generally to canceled claims 17 through 41 and 43 through 46. Claims 42 and 47 are withdrawn from consideration. These new claims add no new subject matter and are fully supported throughout the specification. For the convenience of the Examiner, a marked up copy of the new claims are provided as Attachment A. Support and reasoning for amendments are provided below.

Support for New Claims and Reasons for Amendments

Support for the new claims can be found through the specification, including the drawings and the claims as originally filed. The new claims have been clarified in order to expedite allowance of the present application.

In particular, the recitation in claims 48, 65-68, 72, 74-77, and 80-81 that the cascade genetic circuit is provided in vitro, in gram negative bacteria, or in cultured eukaryotic cell is supported throughout the specification as filed. For example, the field of invention refers to the cascade genetic circuit provided in vitro, in cells, and in cell cultures. Also, at page 4 lines 10 through 13, for example, describe prokaryotic cells such as gram negative bacteria cells, and eukaryotic cells such as mammalian, insect, yeast, and plant cells.

THE CLAIMS AS AMENDED ARE ENABLING UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Applicants' claimed invention is enabling prior to amendment. To expedite the allowance of the application, however, Applicants have provided new claims. Applicants do so without prejudice to pursuing the original claims in another application. Applicants respectfully request that the rejections be withdrawn for the reasons set forth below.

Claims have been amended to clarify that the cascade genetic circuit of the present invention is provided in vitro, in gram negative bacteria, or in cultured eukaryotic cell. As such, enabling supported for the claims can be found throughout the specification as filed. Applicants thus respectfully request that these rejections be withdrawn.

THE CLAIMS PARTICULARLY POINT OUT AND DISTINCTLY CLAIM THE SUBJECT MATTER OF THE INVENTION UNDER 35 U.S.C. §112, SECOND PARAGRAPH

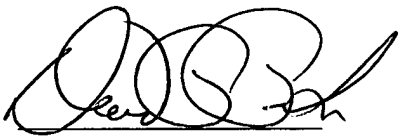
The Examiner asserts that claim 21 (new claim 52) is indefinite in its recitation of "comprises a polypetide." Applicants respectfully disagree, and submit that this claim depends from independent claim17 (new claim 48), which states ". . . a plurality of transcriptional

regulators encoded on one or more nucleic acid constructs . . ." Therefore, because polypeptides rather than nucleic acid sequences may be encoded on one or more nucleic acid constructs, Applicants submit that claim 21 (new claim 52) particularly points out and distinctly claims the Applicants' invention. Applicants thus respectfully request that this rejection be withdrawn.

Applicants respectfully submit that the claims are ready for examination and in condition for allowance.

Respectfully submitted,

Date: Nov 5, 2002



David R. Preston
Reg. No. 38,710

David R. Preston & Associates, A.P.C.
12625 High Bluff Drive, Suite 205
San Diego, CA 92130

Telephone: 858.724.0375
Facsimile: 858.724.0384

ATTACHMENT A

[17.] 48. A cascade genetic circuit, comprising:

a) a plurality of transcriptional regulators encoded on one or more nucleic acid constructs; and

wherein expression of an upstream transcriptional regulator from said plurality of transcriptional regulators stimulates expression of at least one downstream transcriptional regulator from said plurality of transcriptional regulators;

wherein at least two of said plurality of trancriptional regulators are responsive to an inducer;

b) a target promoter;

wherein said target promoter is responsive to a downstream transcriptional regulator of said plurality of transcriptional regulators.

c) wherein said cascade genetic circuit is provided in vitro, in gram negative bacteria or in cultured eukaryotic cell.

[18.] 49. The cascade genetic circuit of claim [17] 48, wherein at least two of said plurality of transcriptional regulators are responsive to the same inducer.

[19.] 50. The cascade genetic circuit of claim [17] 48, wherein said inducer comprises a benzoate derivative.

[20.] 51. The cascade genetic circuit of claim [19] 50, wherein said benzoate derivative is a substituted salicylate molecule or salicylate.

[21.] 52. The cascade genetic circuit of claim [17] 48, wherein at least one of said plurality of transcriptional regulators comprises a polypeptide.

[22.] 53. The cascade genetic circuit of claim [17] 48, wherein at least one of said plurality of transcriptional regulators is encoded by an exogenous nucleic acid molecule.

[23.] 54. The cascade genetic circuit of claim [17] 48, wherein at least two of said plurality of transcriptional regulators are encoded on the same or different exogenous nucleic acid molecules.

[24.] 55. The cascade genetic circuit of claim [17] 48, wherein the expression of at least one of said plurality of transcriptional regulators is modulated by a nucleic acid molecule having the transcription modulating activity of *nahR*.

[25.] 56. The cascade genetic circuit of claim [17] 48, wherein the expression of at least one of said plurality of transcriptional regulators is modulated by a nucleic acid molecule having the transcription modulating activity of *Psal*.

[26.] 57. The cascade genetic circuit of claim [17] 48, wherein the expression of at least one of said plurality of transcriptional regulators is modulated by a nucleic acid molecule having the transcription modulating activity of *XylS2*.

[27.] 58. The cascade genetic circuit of claim [17] 48, wherein said target promoter comprises a nucleic acid molecule having the promoter activity of *Pm*.

[28.] 59. The cascade genetic circuit of claim [17] 48, wherein at least one of said at least two transcriptional regulators regulates the expression of at least one other of said

[29.] 60. The cascade genetic circuit of claim [17] 48, wherein said inducer modulates at least one of said plurality of transcriptional regulators that regulates the activity of said target promoter.

[30.] 61. The cascade genetic circuit of claim [17] 48, wherein the activity of said target promoter is multiplicative.

[31.] 62. The cascade genetic circuit of claim [17] 48, wherein said target promoter regulates the expression of a moiety of interest.

[32.] 63. The cascade genetic circuit of claim [17] 48, wherein said target promoter is operably linked to a nucleic acid molecule that encodes a moiety of interest.

[33.] 64. The cascade genetic circuit of claim [32] 63, wherein said nucleic acid molecule that encodes a moiety of interest is exogenous to a genome or endogenous to a genome.

65. The cascade genetic circuit of claim 48, wherein said cascade genetic circuit is provided in vitro.

66. The cascade genetic circuit of claim 48, wherein said cascade genetic circuit is provided in gram negative bacteria.

67. The cascade genetic circuit of claim 48, wherein said cascade genetic circuit is provided in cultured eukaryotic cells.

[34.] 68. A cell comprising a cascade genetic circuit, wherein said cascade genetic circuit comprises:

a) a plurality of transcriptional regulators encoded on one or more nucleic acid constructs; and

wherein expression of an upstream transcriptional regulator from said plurality of transcriptional regulators stimulates expression of a downstream transcriptional regulator from said plurality of transcriptional regulators;

wherein at least two of said plurality of trancriptional regulators are responsive to an inducer;

b) a target promoter;

wherein said target promoter is responsive to a downstream transcriptional regulator of said plurality of transcriptional regulators.

c) wherein said cell is a gram negative bacteria or a cultured eukaryotic cell.

[37.] 69. The [bacterial] cell of claim [36] 68, wherein said [bacterial] cell is a gram negative bacterial cell.

[38.] 70. The cell of claim [34] 68, wherein said cell is a cultured eukaryotic cell.

[39.] 71. The cell of claim [38] 68, wherein said eukaryotic cell is selected from the group consisting of mammalian cells, insect cells, yeast cells and plant cells.

[40.] 72. A method regulating the expression of a nucleic acid molecule, comprising:

a) providing or establishing a cascade genetic circuit;

b) placing said nucleic acid molecule under control of a target promoter; and

c) inducing said cascade genetic circuit to regulate the expression of said nucleic acid molecule.

wherein said cascade genetic circuit is provided in vitro, in gram negative bacteria or in cultured eukaryotic cell.

[41.] 73. The method of claim [40] 72, wherein said nucleic acid molecule encodes a moiety selected form the group consisting of a hormone, an enzyme, a growth factor, a apolipoprotein, a therapeutic protein, a diagnostic molecule, a diagnostic protein, a diagnostic reporter molecule, a reporter molecule, an anti-sense molecule, a ribozyme, an rRNA, a tRNA, an snRNA, and portions or derivatives thereof.

74. The method of claim 72, wherein said cascade genetic circuit is provided in vitro.

75. The method of claim 72, wherein said cascade genetic circuit is provided in gram negative bacteria.

76. The method of claim 72, wherein said cascade genetic circuit is provided in cultured eukaryotic cell.

[43.] 77. A method of making a moiety, comprising:

a) providing or establishing a cascade genetic circuit;

b) placing a nucleic acid molecule that encodes a polypeptide under control of a target promoter; and

c) inducing said cascade genetic circuit to regulate the expression of said

polypeptide.

Wherein said cascade genetic circuit is provided in vitro, in gram negative bacteria or in cultured eukaryotic cell.

[46.] 78. The method of claim [43] 77, wherein said nucleic acid molecule encodes a moiety selected form the group consisting of a hormone, an enzyme, a growth factor, a apolipoprotein, a therapeutic protein, a diagnostic molecule, a diagnostic protein, a diagnostic reporter molecule, a reporter molecule, an anti-sense molecule, a ribozyme, an rRNA, a tRNA, an snRNA, and portions or derivatives thereof.

79. The method of claim 77, wherein said cascade genetic circuit is provided in vitro.

80. The method of claim 77, wherein said cascade genetic circuit is provide in gram negative bacteria.

81. The method of claim 77, wherein said cascade genetic circuit is provide in cultured eukaryotic cell.